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Wound Healing in Anemia

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EXTENSIVE EXPERIMENTAL EVIDENCE shows that normovolemic anemia is not detrimental to wound healing and need not be corrected simply to assure good repair. The application of these data to patients remains controversial for two reasons: surveys of human healing, largely studies of dehiscence of abdominal wounds, have yielded conflicting results[1]; and common sense decrees that at some point anemia must be detrimental.[2] This issue, the degree of anemia that can be tolerated by patients postoperatively without a sacrifice in healing, has never been investigated. Studies in animals have shown that packed-cell volumes as low as 15% to 20% are compatible with normal development of tensile strength provided that blood volume remains normal.[2,3] This figure seems unacceptably low to many surgeons.

Resistance to the notion that wounds heal well in patients with anemia is understandable. Red cells carry oxygen and oxygen is necessary for wound healing. Several studies have linked the concentration of inspired oxygen with the rate of collagen formation and change of tensile strength in several types of wounds.[4,5] The clinical suspicion that a low hematocrit must retard healing is clearly justified.

The issue needs resolving because the risk of transfusions has dramatically increased with the appearance of the acquired immunodeficiency syndrome. Unfortunately, a prospective study in humans to determine the lower limit of "acceptable" anemia is not feasible. Therefore, we recently took the rare opportunity to study a patient with a packed-erythrocyte volume of less than 20% who required an operation on two occasions. The resulting data directly address this issue, and we submit this report as an indication that in healthy persons, transport of oxygen to wounds and collagen synthesis in them can be supported at normal levels despite a very low red cell mass; and that there is a lower limit of "acceptable anemia."

ABBREVIATIONS USED IN TEXT

Po_2 = oxygen partial pressure (tension)
PTFE = polytetrafluoroethylene

Report of a Case

The patient, a 42-year-old woman with sickle cell anemia, was admitted for treatment of a persistent leg ulcer that was unresponsive to medical management. Her medical history had been complicated by many sickle cell crises and peptic ulcer disease. She had had many transfusions, and cross-matching transfusions for her was difficult. Her preoperative hematocrit was 17.7% (her usual level) with a mean corpuscular volume of 96 cu microns, a mean corpuscular hemoglobin of 33.9 pg and a mean corpuscular hemoglobin concentration of 35.3 grams per dl. Informed consent to participate in the tissue oxygen tension and wound healing studies was obtained preoperatively.

The leg ulcer was excised and the defect covered with a transposition soleus muscle flap and a split-thickness skin graft. She was given two units of packed erythrocytes during the procedure. Intraoperatively, according to established protocol, a small Silastic catheter and two polytetrafluoroethylene (PTFE) tubes were implanted longitudinally in the subcutaneous tissue overlying her upper arm (Figure 1). Oxygen tensions were measured daily in the Silastic tube for seven days after her operation. She was vigorously hydrated with saline, and her tissue oxygen tension on the first day was maintained in the range of 80 to 100 torr, at an inspired oxygen concentration of 50% to 60%. This is an excellent level even for patients who do not have anemia.[5] On the second postoperative day, the tissue oxygen tension fell to 40 torr despite the fact that the patient was breathing oxygen, a low value for postoperative day two. Arterial blood gases (partial oxygen pressure [Po_2] 108 torr, partial carbon dioxide pressure 40 torr, pH 7.38) showed no pulmonary defect. The hematocrit was 13.8%. A 500-ml bolus of normal saline was given over 30 minutes, our usual challenge to

(Jensen JA, Goodson WH III, Vasconez LO, et al: Wound healing in anemia. West J Med 1986 Apr; 144:465-467)

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This study was supported by National Institute of General Medical Sciences grant No. 27345 and a California Heart Association Fellowship (Dr Jensen).

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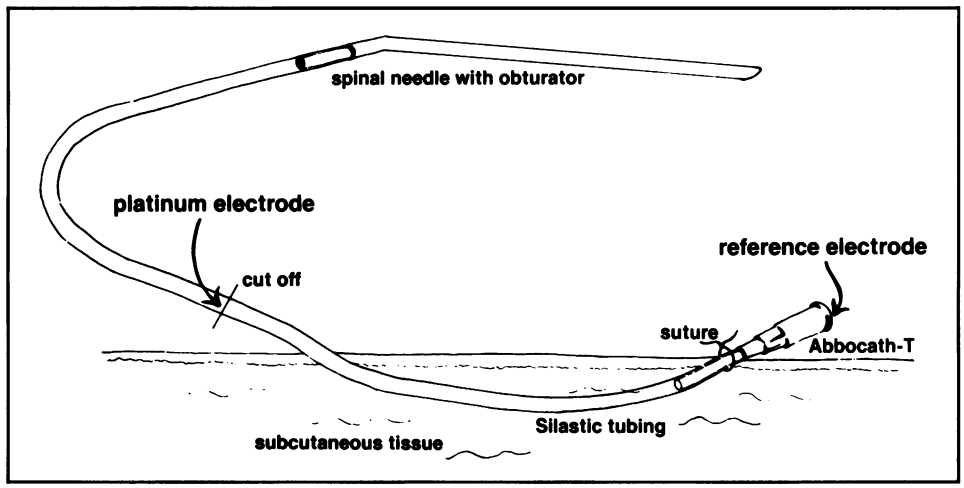

Figure 1.—Tissue oxygen tension is polarographically measured in a subcutaneous Silastic tube using a platinum electrode and a silver-silver chloride reference electrode. When a constant voltage is applied, current is proportionate to oxygen tension.

detect malperfusion due to hypovolemia, but the tissue oxygen tension remained low (44 torr). An electrocardiogram was unchanged from the preoperative recording. Two units of packed erythrocytes were then transfused over six hours. Tissue oxygen tension following the second unit of packed cells rose to 100 torr. Repeat arterial blood gas measurements revealed a Po_2 of 112 mm of mercury. Her hematocrit was then 20.2%. She then maintained normal blood and tissue oxygen levels and a hematocrit of approximately 20% through postoperative day seven.

The PTFE tubes were withdrawn on the fifth and seventh postoperative days. Collagen deposition was measured as previously described[6] and was 4.28 μg per cm. This is above the mean but within one standard deviation (3.24 ± 1.56) of values from a population of similarly treated postoperative patients ($N = 31$), all of whom had higher hematocrits.

The patient recovered from her operative procedure uneventfully. Her surgical wound healed well, with nearly 100% take of the split-thickness skin graft. The ulcer has not recurred during 18 months of follow-up care. Gangrenous cholecystitis developed 16 months later, and an emergency cholecystectomy was done. Her hematocrit was in the low 20s. Tissue oxygen tension studies were again done and remained in the normal range. She had a "healing ridge" by five days and has suffered no wound morbidity at two months after the procedure.

Discussion

Studies in anemic animals in which blood volume was maintained have consistently failed to show defects in wound healing. Furthermore, wound oxygen tension in control and anemic animals remains normal throughout a range of hematocrits from 30% to 40%, and collagen deposition is slightly greater at the lower level.[7] Most studies implicating anemia as a cause of poor healing have been discredited because correction of the hypovolemia or malnutrition that was coincident with the experimental anemia also corrected the deficit in repair. As the hematocrit in normovolemic and well-ventilated patients continues to fall, however, a point must be reached at which oxygen-carrying capacity is no longer sufficient to maintain Po_2 in the capillaries. Tissue oxygen tension must then be depressed, and the oxygen-carrying capacity must at that point become a limiting factor in wound healing. Zederfeldt, in a study using animals, estimated this point, the critical range of hematocrit, at about 15%.[3]

This patient's wound oxygen tension fell when her hematocrit fell from 17% to 14%. Because her tissue Po_2 was unresponsive to fluid challenge, transfusion of erythrocytes seemed necessary. During transfusion of packed cells, and as the hematocrit reached 20%, the tissue oxygen tension increased from 40 to 100 torr while the patient breathed 50% to 60% oxygen. These data suggest that a "critical hematocrit" between 14% and 20% existed for this patient.

We have monitored tissue oxygen tension in four other patients with anemia (three sickle cell, one hemolytic) who had hematocrits in the range of 20%. All had normal tissue oxygen tension except when blood was removed for exchange transfusion. Changes of hematocrit in the range of 18% to 28% were not accompanied by either rising or falling wound tissue Po_2.

Tissue oxygen measurements should be particularly important in patients with homozygous sickle cell disease, in whom capillary hypoxia is thought to polymerize hemoglobin S, rendering erythrocytes rigid and creating a cycle of increasing hypoxia.[8] Aggressive fluid administration is standard therapy. Occasionally, however, erythrocyte transfusions seem necessary. The patient in the case reported here had no symptoms of sickle cell crisis, but sickling may have contributed to her tissue hypoxia. Transfusion may also affect the periodic microcirculatory flow seen in patients with sickle cell disease.[9] It seems possible that the "critical" level of hematocrit in this patient might be higher than in patients with less complex anemia.

Though collagen deposition in PTFE tubes has not yet been correlated with a clinical index of healing of the surgical wound such as dehiscence, fibroblasts migrate into the PTFE tubes and deposit collagen there, as they do in healing surgical wounds.[10] The technique has shown significant healing defects in patients with uremia and in smokers.[11,12] This patient deposited a high-normal amount of collagen in the PTFE tubes, even on a standard derived from 31 postoperative patients, all of whom had higher hematocrits.

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An Unusual Case of Tuberculous Peritonitis in a Man With AIDS

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PATIENTS with the acquired immunodeficiency syndrome (AIDS) are known to be susceptible to mycobacterial infections because of their defective cell-mediated immunity. When tuberculosis occurs in these patients, it is often extrapulmonary.[1] We describe a case of a patient with Kaposi's sarcoma in whom an intra-abdominal tuberculous abscess developed. To our knowledge, this complication has not been previously reported in patients with AIDS.

(Barnes P, Leedom JM, Radin DR, et al: An unusual case of tuberculous peritonitis in a man with AIDS. West J Med 1986 Apr; 144:467-469)

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Report of a Case

The patient, a 37-year-old homosexual man, presented to a physician with a one-day history of severe abdominal cramps, constipation and a temperature of 40°C (104°F). He had had fever, fatigue and weight loss for five weeks. The physician noted purplish papules over his chest and abdomen. He was admitted to another hospital, where a biopsy of the skin lesions revealed Kaposi's sarcoma. A plain film of the abdomen showed splenomegaly and a poorly defined left lower quadrant mass. A contrast enema examination showed no abnormalities and a gallium scan disclosed a focal area of increased activity at the level of the iliac crest to the left of the midline. Computed tomography (CT) showed a 7-cm diameter heterogeneous mesenteric mass in the left lower quadrant, with a low-density central area (Figure 1). Mesenteric and retroperitoneal lymph nodes were slightly enlarged. Splenomegaly and thickening of the mesentery were also noted. The patient was transferred to our hospital for further evaluation.

On examination, the patient was noted to be thin but apparently was in no acute distress. His temperature was 40.1°C (104.2°F), blood pressure 119/62 mm of mercury, pulse 90 and respirations 16 per minute. Several purplish papules less than 1 cm in diameter were noted over his chest, abdomen and lateral neck. There was shotty cervical, axillary and inguinal adenopathy. The spleen tip was palpable and tender. No masses were palpable and there was no evidence of ascites. The rectal tone was diminished.

A radiograph of the chest was normal. The hemoglobin was 11.6 grams per dl, with a mean corpuscular volume of 78.2 cu microns. There were 6,100 leukocytes per μl, with 71% segmented neutrophils, 3% band forms, 15% lymphocytes and 11% monocytes. Results of a urinalysis, serum electrolyte levels, creatinine level and results of liver function tests were all normal except for the total protein and albumin levels, which were 6.7 and 3.5 grams per dl, respectively. Blood, sputum, urine and stool cultures yielded no pathogens

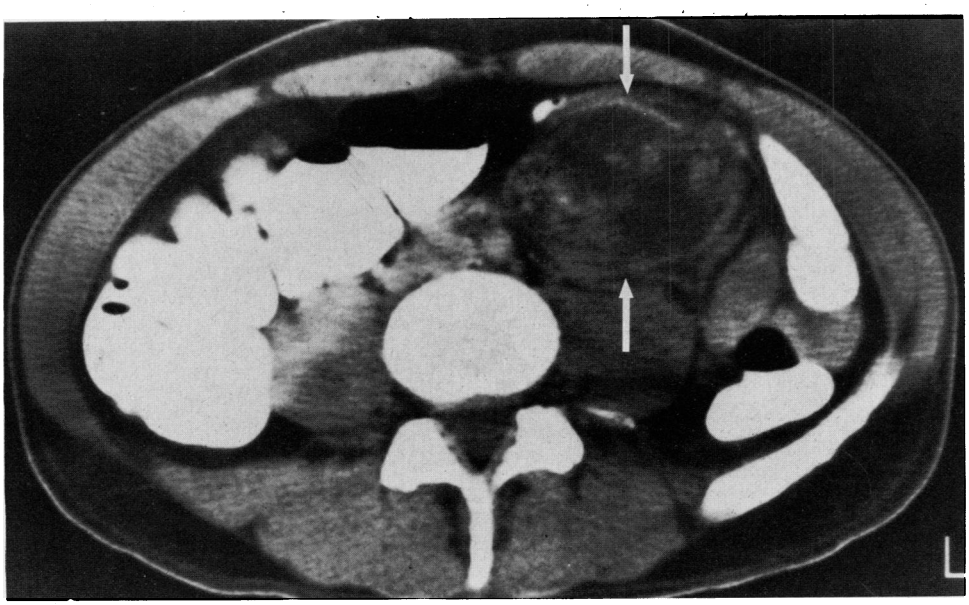

Figure 1.—A computed tomographic scan shows a mesenteric mass **(arrows)** containing areas of soft tissue and water density. There is a surrounding rim of soft tissue.